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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/658,862	09/08/2000	Keith Henry Stockman Campbell	SP-02-US-DIV-1	2555

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
08/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SAL@ARRIGO.US

Office Action Summary	Application No.	Applicant(s)	
	09/658,862	STOCKMAN CAMPBELL ET AL.	
	Examiner	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *163 and 168-171* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *163 and 168-171* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/803,165.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments filed May 25, 2009 have been fully considered but they are not persuasive. Claims 163 and 168-171 are pending.

Applicant has request clarification as to the reasoning behind an enablement rejection and an anticipatory rejection over the same claims. The enablement rejection is based on the lack of an enabling disclosure for the production of a "cloned" mouse, rabbit, rat or horse. The term "cloned" is recognized by the art has being produced by a nuclear transfer method. The anticipatory rejection is based on the lack of a patentable distinction between the claimed cloned mouse, rabbit, rat or horse and the prior art mice, rabbit, rat or horse.

The terminal disclaimer filed on May 25, 2009 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent 7,232,938; U.S. Patent No. 7,304,204 ; U.S. Patent 7,307,198 ; U.S. Patent 7,321,076 ; U.S. Patent 7,326,824 ; U.S. Patent 7,326,825 ; U.S. Patent No. 7,332,648 ; U.S. Patent 7,355,094; U.S. Patent No. 7,361,804 and 7,432,415. in the office action mailed November 26, 2009 has been reviewed and is accepted. The terminal disclaimer has been recorded. Please note U. S. application serial no. 11/068,903 has now issued as U.S. Patent 7,432,415,

The nonstatutory double patenting rejection made in the office action mailed November 26, 2009 over the claims in U.S. application serial no. 11/543,786 and U.S. application serial no. 11/544,038 is withdrawn as these applications are now abandoned.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 163 and 168-171 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter for reasons set forth in the in the office action mailed November 26, 2008. Claims 163 and 168-171 are drawn to a live born clone of a pre-existing, non-embryonic, donor mammal, wherein the mammal is selected from mice, rabbits, horses and rats. However, the claimed mammals do not sufficiently distinguish over pre-existing mice, rabbits, horses and rats. Neither the claims nor the specification point out any structure or phenotype that separates cloned mice, rabbits, horses and rats from pre-existing mice, rabbits, horses and rats. The method of making the mammals does not imbue any new or novel characteristic to the cloned mammals nor does the method imbue a new use to the mammals claimed. Further, the claims clearly state that the clone is a copy of a pre-existing mammal. Hence, the mammal as claimed is indistinguishable from the mammal as found in nature. Thus, the cloned mice, rabbits, horses and rats of the claims is not seen as being "new" as required by 35 U.S.C. § 101.

It is well known and accepted that patentability is precluded for certain subject matter, products of nature, natural phenomenon, being one of them. The claimed cloned mice, rabbits, horses and rats were, as disclosed in the specification, indeed, produced by a method that has the hand of man associated with it. However, the question raised under 35 U.S.C. § 101 relates to the patentability of subject matter that occurs in nature, is a copy of a product of nature, but the copy was created by the hand of man. Does the hand of man extend through the method to the product?

Applicant argues mammals do not naturally reproduce by cloning, and a cloned mammal within the scope of applicant's claims is a non-naturally occurring product of human ingenuity. Applicant states the claims are not to a product of nature but one that is made by man. This argument is not persuasive.

Applicant's method surely is the hand of man and is statutory subject matter, but what applicant's method makes is a natural product. If applicant's argument is true, then mammals produced by IVF would be patentable over mammals produced by mating.

Applicant argues if the examiner's argument that the claimed clones are products of nature because a naturally occurring female was used in the process, then many if not all recombinant products would be considered "products of nature." Applicant argues the Supreme Court held in Diamond V. Chakrabarty, statutory subject matter includes "anything under the sun that is made by man." Applicant reiterates the argument that the cloned mammals claimed are made by man because the cloning process is a man-made process. This argument is not persuasive.

In Diamond V. Chakrabarty, the Supreme Court found genetically engineered microorganisms as statutory subject matter. The fact that the microorganisms contained a gene sequence that naturally they did not contain, the Supreme Court stated this fact indicated human intervention providing the microorganisms with statutory status. The Supreme Court did not address replicas of wild-type, naturally occurring organisms such as applicant's claimed cloned mammals.

With regard to Diamond V. Chakrabarty, one test of statutory subject matter is found in MPEP 2105: (B) A "nonnaturally occurring manufacture or composition of

matter - a product of human ingenuity -having a distinctive name, character, [and] use" is patentable subject matter. However, if we accept “clones” as not naturally occurring, the cloned mammals claimed do not have a distinctive name, character and use. The clones have the same name, character and use as the nucleus donor mammal. Thus, Diamond V. Chakrabarty supports the nonstatutory category of the claimed invention.

Applicant further argues “new” is not relevant to an analysis of statutory or nonstatutory subject matter. Applicant cites In re Bilski with reference to “new.” This argument is not persuasive.

The court in Bilski states “Congress did not intend the “new and useful” language of § 101 to constitute an independent requirement or novelty or nonobviousness." It is noted that on this record, applicant has several times stated the cloned mammals are replicas or copies of known mammals. Thus, even in view of the court's statement in Bilski, a replica or a copy of a known product is not “new” within the meaning of 101. The closest comparison is IVF. If applicant's clones are statutory subject matter, then IVF produced mammals would be also, and those mammals produced by artificial insemination. In each of these methods, cloning, IVF and artificial insemination, the products produced are products of nature. They have no different use or structure over those mammals known in the art at the time of the invention. A cloned mammal, viewed as a replica or a copy, is not "new.”

Applicant has never states what the *new* is regarding the cloned mammals claimed. A new way of making a product does not give the product "new" features

necessarily. The method could provide new features to the product, but in the present prosecution no new features, characteristics, structure have been provided.

Applicant argues anticipation can only be found when the reference discloses exactly what is claimed. Applicant argues when differences between the reference and the claims occur, the rejection must be based under 35 U.S.C. § 103. Applicant argues the fact that the clone and the parent are different, as conceded by the Examiner, precludes anticipation of application's claims. These arguments are not persuasive.

First, any differences between the cloned mammals and the prior art references are those that do not affect the structure or function of the mammal. The differences are immaterial and do not patentable distinguish between cloned mammals and those known in the art at the time of filing. As stated, given applicant's rationale, a cow with a twisted horn would be patentable over a cow with a normal horn, as long, one presumes, as the cow was made by IVF, artificial insemination or cloning. This reasoning does not follow the case law of product by process, which gives lenience in old products produced by a new method for differences that do not affect the structure or function of the product. Applicant has not set forth any differences that would provide patentability of the cloned mammals over those known in the art at the time of filing. How they are the same has repeatedly been set forth, but applicant has not explaining or provided evidence that the cloned mammals and mammals in the art at the time of filing have any differences that make them patentably distinct, that provide the cloned mammals with “a distinctive name, character, [and] use" as required by Diamond V. Chakrabarty.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 163 and 168-171 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons set forth in the office action mailed November 26, 2009. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. At the time of filing, the skilled artisan would have regarded the cloning of mice, rabbits, horses and rats to be unpredictable. Each used method steps not taught by the present specification.

At the time of filing, the skilled artisan would have regarded the cloning of mice, rabbits, horses and rats to be unpredictable. Each of the references discussed used method steps not taught by the present specification in the successful SCNT production of cloned mice, rabbits, horses and rats.

Applicant argues the delayed activation procedure of Wakayama is described in Applicant's specification. Applicant argues the examiner has mischaracterized the specification by stating the disclosure requires the reconstituted embryos need to be incubated in the presence of a microtubule destabilizer. Applicant argues the conclusion of Ogura that delayed activation is important for cloning mice refers to cloning mice with somatic cells. These arguments are not persuasive.

The examiner maintains that the specification states the need for incubation in the present of a microtubule inhibitor during delayed activation. The specification states this leads to the inhibition of spindle formation and preventing mitosis. The specification also states the inhibitor should be added "a sufficient time before activation to ensure complete, or almost complete, depolymerization of the microtubules." (See specification, page 14, lines 21-28.) This indicates the specification teaches using a microtubule destabilizer during delayed activation. Ogura indicates, as stated by applicant, SCNT for mouse requires delayed activation. Also it is noted, the present specification provides very broad disclosures for nuclear transfer, without any particular direction for mice, rabbits, horses or rats. As such the specification is more of a list of suggested methodologies with little true guidance for the artisan. Thus, there is an undue amount of experimentation associated with the claimed invention and without a predictable degree of success.

Applicant argues the methods of Landa et al and Al-Hasani et al would have been known to the artisan at the time of filing as these two publications were published prior to the present effective filing date. Applicant argues that cloning (nuclear transfer) and IVF are materially different methods is not relevant. Applicant argues the success of a particular technique does not indicate it is required or that other techniques will not work. This argument is not persuasive.

Chesne states there were no clone rabbits produced by nuclear transfer prior to their experiments. Thus, Chesne is saying the use of asynchronous recipient female rabbits and recipient oocytes is necessary. Further, as previously cited on this record,

Pennisi provides additional evidence that the production of rabbits is required undue experimentation at the time of filing without a predictable degree of success. Pennisi stated that rabbits had eluded cloning in spite of their reputation for fecundity (page 1725, col. 2). Thus the knowledge in the art would have led the skilled artisan to find the production of cloned rabbits to be unpredictable under the standards of Wands (In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

Applicant argues the spontaneous activation characteristic of rat oocytes was well known in the art at the time of filing. Applicant provides Keefer (1982) as evidence of this. Applicant argues that at the present effecitve filing date, the skilled artisan would know to produce rat oocytes for nuclear transfer methods, the oocytes would have to be removed and cultured as quickly as possible to avoid spontaneous activation. These arguments are not persuasive.

Even when using a nuclear transfer method that involved the quick removal of oocytes from rat ovaries, no clones were produced. The problem with rat somatic cell nuclear transfer is due to the spontaneous activation of rat oocytes within 30 minutes of their removal from the oviduct (Zhou, page 1179, col. 1, parag. 2, lines 5-10). Even when a “speedy” enucleation and transfer method was developed, no clones were born (Zhou, col. 2, lines 3-6 and parag. 1, lines 4-7). Therefore the suggestion of Keefer that a quick recovery and culture of rat oocytes inhibits oocyte activation would not enable the invention. These teachings are evidence of the unpredictability under the Wands factors of the claimed invention of live-born cloned rats, as opposed to the need for routine experimentation.

Applicant argues a major factor in horse cloning is the availability of horse oocytes, citing Lagutina et al (2005). Applicant argues the low availability of horse oocytes does not equate with a lack of enablement. Applicant also argues neither inhibiting protein synthesis nor phosphorylation at the oocyte activation stage, nor is zona-free manipulation of oocytes critical for cloning horses. Applicant argues Hinrichs (1995) teaches indicates a combination of a calcium ionophore with cycloheximide, a protein synthesis inhibitor, but lacking a phosphorylation inhibitor, resulted in 49% activation of equine oocytes. Applicant argues the combination of a calcium ionophore with a protein synthesis inhibitor was known prior to the present effective filing date to be sufficient for horse oocyte activation. Applicant also argues horse oocytes can be activated by other protocols using a calcium ionophore and a protein synthesis inhibitor, a calcium ionophore and a phosphorylation inhibitor, or ionomycin, a protein synthesis inhibitor or a phosphorylation inhibitor. Applicant argues although the latter protocol was three-fold more efficient. Efficiency, applicant argues is not a requirement for enablement. Further, applicant argues the zona-free manipulation only increases efficiency of embryo reconstruction, but this manipulation is not necessary for horse cloning. Applicant also argues Woods (2003) teaches the cloning of a mule using a horse oocyte, where the oocyte was zona intact. This applicant argues proves zona free oocytes are not required to produce horse clones. These arguments are not persuasive.

While efficiency may not be required for enablement, a predictable method without an undue amount of experimentation is required. The references Lagutina, and Hinrichs show horse oocyte activation, but there is no production of cloned horses.

Lagutina supports the statements of Galli (2003) of record that these "aides" increased efficiency so that SCNT for cloning horses could be successful, that a live-born horse. Hinrichs provides no evidence a more efficient method of activating horse oocytes would necessarily lead to more cloned horses. As known in the art, and evidence by Pennisi et al, even pregnancy does not lead to a live-born clone (Pennisi and Vogel (2000), page 1722, col. 1, parag. 3, lines 16-18). Thus, by extension, activated oocytes would not have been regarded by the skilled artisan at the time of filing to necessarily lead to a cloned mammal. In addition, Choi, of record, shows, using a method very similar to applicant's disclosed method, failed to produce NT embryos for transfer. This indicates horse nuclear transfer is unpredictable, requiring methods not taught by the present specification.

As for the production of a cloned mule using horse oocytes, Woods states the calcium levels in horse oocytes were lower as compared to bovine oocytes. Thus, the calcium levels were increased in horse oocyte culture media (Woods, page 1063, col. 1, parag. 2, lines 15-20). Elevation of extracellular calcium concentrations may have contributed to the successful equine nuclear transfer according to Woods (Woods, page 1063, col. 2, parag. 1, lines 1-6). Thus, Woods supports the arguments and evidence sent forth in this prosecution that the present specification does not enable the production of cloned horses.

In the art rejections below, the rejections have been made under 35 U.S.C. § 102/103. The phrase "live-born clone of a … mammal" imbues the method by which the clone was made, nuclear transfer.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skills in the art to which said subject matter pertains. patentability shall not be negatived by the manner in which the invention was made.

Claims 163 and 168 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Eppig et al. (1989) Biology of Reproduction, Vol. 41, pp. 268-276 for reasons set forth in the office action mailed November 26, 2009.

Eppig teaches live-born mice produced by in vitro fertilization (IVF) (peg 274, col. 1, parag. 2 to col. 2, line 5).

Claims 163 and 169 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Brackett et al. (1975) Biology

of Reproduction, Vol. 12, pages 260-274 for reasons set forth in the office action mailed November 26, 2009.

Brackett teaches live-born rabbits produced by in vitro fertilization (IVF) (page 269, col. 2, lines 9-15).

Claims 163 and 170 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Palmer et al. (1991) Journal of Reproduction and Fertility Supplement, Vol. 44, pages 375-384 for reasons set forth in the office action mailed November 26, 2009.

Palmer teaches the production of live-born horses by in vitro fertilization (IVF) (page 382, parag. 2).

Claims 163 and 171 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Toyoda et al. (1974) Journal of Reproduction and Fertility, Vol. 36, pages 9-22 for reasons set forth in the office action mailed November 26, 2009.

Toyoda teaches the production of live-born rats by in vitro fertilization (IVF) (page 19, parag. 1, lines 1-4).

With regard to prior rejections made under 35 U.S.C. § 102/103, applicant argues for anticipation the identical invention must be shown in as complete details as contained in the patent claims and requires the presence in a single prior art disclosure all the elements of a claimed invention. Applicant argues, generally, the prior art did not show the production of a clone of a pre-existing, non-embryonic donor mammal. Applicant argues this omission in the prior art precludes the present claims from being

anticipated. Applicant further argues the mammals in the prior art would have the genetic complement of two parents, not just one, the parent being the nuclear donor. These arguments are not persuasive.

The rejection here is based on patentably indistinctness between the claimed clones of pre-existing mice, rabbits, horses and rats. There is no disclosure in the present specification that directs the determination of a cloned mouse, rabbit, horse or rat from those of the cited prior art. Neither the specification disclose any new feature or characteristic of the cloned mice, rabbits, horses, and rats from those made by IVF. As such applicant's clones are the same as the mammals known in the art at the time of filing. Applicant has a new method for producing an old product. While having been made by a method of nuclear transfer (cloning) enables the art to produce inexact copies of pre-existing mammals, the method does not alter the mammal itself. The statements made by declarant, relate to the method, not the mammal. Coexistence, time-delayed, inexact copy are all traits of the method. The mammal produced by such a method cannot be distinguished from any other wild type mammal of the same species. Applicant should clearly state how such a distinction can be made. The only imaginable means to make a distinction would be to review breeding records to determine how the mouse, rabbit, horse or rat was produced. This, however, does not impart a novel trait the mouse, rabbit, horse or rat in question.

Applicant argues the cited references are missing an element as recited in applicant's claimed invention, to cloned mammals. Applicant argues the cited prior art references do not disclose a clone. Applicant further disagrees with the examiner's

interpretation of the claims as a product by process. Applicant argues the claimed mammals are not product by process and are not limited to any particular method. These arguments are not persuasive.

The term “clone” means the mammal claimed was made by a particular process, a cloning process. This is the interpretation and common usage in the art. The ordinary artisan reading the present claims would realize the mammals had been made by a cloning method. In this regard, the claims are product by process just as the term "recombinant protein" indicates the protein was made by methods of recombinant technology.

Applicant argues the mammals taught in the cited prior art references are to mammals produced by in vitro by IVF using sperm and an egg. Applicant argues the mammals were produced by sexual reproduction and are not clones. Applicant argues the IVF produced mammals are not identical to either of its parents, but only 50% identical to each of them. These arguments are not persuasive.

There is no definition of “identical” in the specification. Two cows can certainly look identical and have identical structure and function. "Identical” cannot mean identical DNA sequences, as even human monozygotic twins have DNA sequence mutations (). There is no evidence that cloned mammals have the exact same DNA sequence as the nucleus donor mammal. Given the twin data, it is apparent they don’t. So, if the clones are not DNA sequence identical to the donor, then how are they identical? They have the same number of chromosomes and the same gene set. If we decide clones can have some differences between them and their nuclear donor, then, 50% of the DNA

will not match both parents. Applicant states the clone can be distinguished from the IVF produced mammal by DNA analysis. Why type of DNA analysis? Sequencing the genome of the mammal may show silent nucleotide substations, additions and deletions. Hybridization analysis would not distinguish as the genes are the same between mammals of a given species. RFLP analysis would not necessarily detect the clone if the IVF mammal was related or if the clone had a mutation that caused a different RFLP pattern from the nuclear donor. Thus, the examiner maintains a cloned mammal and a mammal of the prior art are not patentably distinct because there is no structural or functional difference between them, or any difference does not affect the structure or function of the clones vs. IVF produced mammals. Applicant has not provided any evidence that the clones and the IVF produced mammals are different in any manner except the method used to make them. Absent a definition of "identical" in the specification, the ordinary artisan would realize that a cloned mammal and an IVF mammal are identical under the premise of 35 U.S.C. § 102(b) and 35 U.S.C. § 103. In a site by side comparison, there is no difference between a cloned mammals and an IVF mammal.

Applicant argues there is no art that demonstrates the cloned mammals of the claims and those mammals in the prior art have the same nuclear genetic code. Applicant also argues clone can be identified from a non-clone by DNA analysis using techniques routine in the art. These arguments are not persuasive.

The specification provides no evidence or guidance as to determining if the clone and the donor are "genetically identical." The means of determining such sameness is

not clear and, at least by microstatellite analysis, is dependent upon experimental factors. Microsatellite analysis is dependent on the number of markers observed. More differences are seen using more markers. MacHugh performed micro satellite analysis on seven breeds of bovines (page 338, Table 2). The analysis showed the ability to assign a particular bovine to a particular breed varied in relation to the number of microstatellite markers used. For example, in experiments for bovine breed assignment, fewer markers fail to show breed differences, and thus more breed assignment overlap. Use of 4 markers showed identical patterns between A. Angus and Hereford, Jersey, Kerry, Charolais and Friessian. As the number of microstatellite makers analyzed increased, the overlap in herd assignment decreased (as example, see page 338, Fig. 2, A. Angus across for each number of microsatellite markers). Thus, two lessons are learned from this data.

The first is the genotype of any mammal as compared to another mammal, such as a clone and the nuclear donor, is dependent upon the number of microsatellite markers analyzed. The more markers the greater the likely hood for establishing or not establishing the degree of genetic identical-ness. Thus, saying the clone is a genetic identical to the nuclear donor is dependent upon the number of microsatellite markers, or other genetic markers, examined. Thus, in Dolly, four microsatellite markers were examined. Given the date of Mac Hugh, four markers may miss a genetic difference. There is no data on this record to indicate a clone and the nuclear donor are genetically identical as there is no clear evidence that such has been established, and no clear

guidance on the criteria for determining if a cloned mammal is genetically identical the nuclear donor.

Second, the data present in MacHugh shows that within a single bovine breed, microstatellite markers demonstrate genetic sameness. A. angus, Hereford, Jersey and Kerry exhibited the same marker pattern 100% or 99% of the time. This means within a breed, the microstatellite markers exhibit the same pattern in the individual members of the breed. MacHugh, it should be remembered, set about to establish marker patterns associated with particular breeds. Thus, MacHugh demonstrates all members of a breed can be genetically identical. Therefore, the clone cannot be shown to be produced from any particular member of the same breed by microstatellite analysis. Based on this, analysis of clone's genome will not identify the nuclear donor or even determine a clone from a mammal produced by IVF, artificial insemination or mating.

In summary, the data of MacHugh shows members of a given breed are genetically identical. Thus an Angus clone cannot be distinguished from another Angus, unless that Angus has some mutation. The specification fails to provide a particular recombinant DNA method, as stated by applicant that provides individual genetic distinction. In addition, as genetically identical has no clear definition in the specification and the specification fails to provide guidance for determining genetic identical-ness, the cited prior art anticipates the claimed invention.

Further, the mammals of the cited prior art all each from an inbred strain or breed. Inbreeding means "the mating of two closely related persons. Also called consanguinity. The act of mating closely related individuals. The mating of organisms

between relatives, which usually decreases heterozygosis in the gene pool". Of interest is of 30 million Holstein bovines, Holstein being an inbreed bovine breed, there are only 35-40 different "individuals." This means genetically, there are 35-40 Holstein genotypes. Thus, while the clone could be same genetically identical to the nuclear donor, it could also be genetically identical to another Holstein. The specification provides no guidance that the clone and the nuclear donor are genetically unique from other mammals of the same breed or strain.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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